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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,964	11/26/2001	Franz-Josef Rubroder	02481.1671-01	1450

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EXAMINER

CHERNYSHEV, OLGA N

ART UNIT PAPER NUMBER

1646

DATE MAILED: 07/08/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/991,964

Applicant(s)

RUBRODER ET AL.

Examiner

Olga N. Chernyshev

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-77 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 23-77 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

1. Applicant's election of *Escherichia coli* as the species of host cells in Paper No. 7 is acknowledged. Claims 23-77 are under examination in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 recites the limitation "animal insulin" in claim 45. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-46 and 48-77 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-11 and 16-22 of U. S. Patent No. 6,339,061. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claim is generic and encompasses the subject matter of the patent claims in its entirety. Furthermore, the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent and there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter. Claims 23-46 are directed to a process for the storage of a protein in an aqueous solution, comprising adding an amount of cysteine effective to delay the temporal decrease in the effective concentration of the protein not more than 7%. The limitation of "not more than 7% decrease in the effective concentration" was fully disclosed in the U. S. Patent No. 6,339,061 (see Table 3, column 5, where the effective concentration of the protein in mg/L after 8 weeks of storage is about 93% of that of the first day).

Claims 48-73 are directed to a process for the storage of a protein in an aqueous solution, comprising adding an amount of cysteine effective to delay the temporal decrease in the effective concentration of the protein during a certain period of time (24 hours, 48 hours, 1 week, 2 weeks,

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4 weeks, 8 weeks or more). The limitation of the time period of the storage of the protein in an aqueous solution is fully disclosed in the U. S. Patent No. 6,339,061 (see column 5, Tables 1-4 and lines 59-61).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 23-34, 40-46, 48-64 and 70-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flaa et al. (1996, WO 96/27661) and Mikura et al. (1985, EP 158487) and further in view of Ahmad et al. (1983, JAOCS, 60, 4, pp.837-840) and Santha et al. (1979, Indian J.Anim.Sci., 49, 1, pp.37-41). Copies of the references were provided with an office action of Paper No.3.

Claims 23-34, 40-46, 48-64 and 70-77 are directed to a process of a protein storage in an aqueous solution with addition of cysteine as a reducing agent. The process of addition of reducing agents to proteins and lipids for stabilization and storage purposes is known and well described in the art. Flaa et al. (1996, WO 96/27661) teach compositions for stabilizing proteins in aqueous solutions, which contain, among other ingredients, reducing agents (see the abstract and page 11, first paragraph). Flaa et al. (1996, WO 96/27661) did not expressly use cysteine as a reducing agent for the stabilization of proteins but used cysteine derivative NAC (N-acetylcysteine) (page 11, first line). Mikura et al. (1985, EP 158487) also teach storage of protein (interleukin-2) compositions, which contains a reducing compound (see the abstract and page 3, fifth paragraph). Mikura et al. (1985, EP 158487) did not expressly disclose cysteine as a reducing compound in particular but mentioned cysteine derivatives, such as N-acetylcysteine and N-acetylhomocysteine (page 3, fifth paragraph). Ahmad et al. describe a method of storage of vegetable oils in aqueous solution with antioxidant amino acids, cysteine among them provided the most activity (see the abstract, Figures 1, 2 and Table II). Also Santha et al. describe the stability of ghee (butter) depends on the presence of amino acids, such as cysteine with antioxidant properties (see the abstract and Table 2). Thus, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use cysteine as a reducing agent for the protein storage. One of ordinary skill in the art would have been motivated to do this because, first, cysteine is a well-known reducing agent, which derivatives are widely used as reducing agents, second, can be interchangeably used when a protocol calls for the use of a reducing agent, and, third, is well known to be used for the storage, stabilization and protection of lipid and non-lipid containing compositions. Furthermore, one of ordinary skill in the art

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readily recognizes the advantage to use cysteine as a storage agent/additive to a protein in aqueous solution because it is a naturally occurring amino acid, and one would not expect any side effects from residue cysteine amounts when using the protein in future pharmacological or clinical applications. This is demonstrated by the fact that Ahmad et al. and Santha et al. employ cysteine in the preservation of food. Finally, it would have been obvious for a person of ordinary skill in the art to store a protein in aqueous solution within optimal range of temperatures, such as 0°C to 50°C, because it is common knowledge for storing proteins at these temperatures to avoid degradation or denaturation.

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-0294 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices

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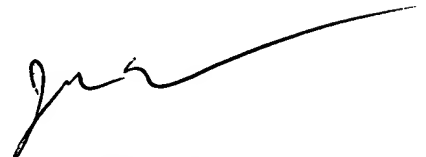
published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
July 3, 2002

OC



JOHN ULM
PRIMARY EXAMINER
GROUP 1000